

The Examiner has acknowledged applicants' claim for foreign priority. The Examiner alleges that Applicants have not filed a certified copy of applications PN-6135, PN-7276 and PO-2208 as required by 35 U.S.C. §119(b).

Applicants respectfully submit that certified copies of the foregoing Australian applications will be filed in due course.

The Examiner has objected to the drawings allegedly because each figure must be described separately in a BRIEF DESCRIPTION OF THE DRAWINGS.

Applicants have amended the BRIEF DESCRIPTION OF THE DRAWINGS, and in particular Figures 1, 3, 4, 5 and 7 to meet the labeling requirements of 37 C.F.R. §1.84(u)(1)

The Examiner has also objected to the application because the word following "is capable of" in claim 17 is not legible.

Applicants respectfully submit that the word following "is capable of" in claim 17 is "interaction". It is submitted, however, that claim 17 has been canceled without prejudice, thereby rendering the objection moot.

The Examiner further alleges that the application fails to comply with the sequence rules 37 C.F.R. §§1.821-1.825. The Examiner alleges that the sequences in Figure 7 are not identified by SEQ ID NOs, and that the sequence on page 31, line 17 is not identified by SEQ ID NO. In addition, the Examiner alleges that claims 1-2 refer to an amino acid sequence without reference to a sequence identifier.

In response, Applicants have amended the Brief Description of the Figures for Figure 1 to include reference to SEQ ID NO: 9 at page 31, line 17, which corresponds to the sequence identified as "WSXSW". Applicants have also amended the Brief Description of the Figures for Figure 7 at page 32, line 20, to include reference to SEQ ID NOS:1-4, and for Figure 10 to

include reference to SEQ ID NOS:10 and 11. Furthermore, Applicants have amended the specification at page 37, line 5 to include reference to SEQ ID NO: 12, which corresponds to the sequence identified as "Trp-Ser-Asp-Ser-Trp". A substitute sequence listing reflecting SEQ ID NO: 12 is also provided. No new matter has been added.

As to the sequences referenced in claims 1-2, these claims have been canceled without prejudice and reference to sequence identifiers in these claims is therefore not necessary.

In the claims, Applicants respectfully direct the Examiner's attention to the amendments to the claims. Claims 16-17 have been canceled without prejudice, in response to the Restriction Requirement. Applicants reserve the right to file a divisional application directed to the subject matter of these canceled claims. Claims 18-19 have also been canceled without prejudice in favor of the added claims 36-50. Specifically, claim 36 is directed to an isolated antibody generated using an IL-13 receptor α -chain polypeptide comprising all or part of SEQ ID NO: 4, which antibody binds to an IL-13 receptor α -chain. Claim 37 is drawn to an isolated antibody which binds specifically to an IL-13 receptor α -chain consisting of the sequence of SEQ ID NO: 4. Support for claims 36-37 is found in the specification, e.g., at page 22, lines 7-9; and page 7, lines 1-3. Claims 38-42 depend upon claim 36 or 37 and further delineate various features of the preferred antibodies of the present invention. Support for claims 38-42 is found in the specification, e.g., page 27, lines 25-28. Claims 43-48, depend from claims 36-42, are drawn to pharmaceutical compositions comprising an isolated antibody of the present invention. Claims 49-50 are drawn to an isolated antibody against an IL-13 receptor α -chain or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment binds SEQ ID NO: 4. Support for claims 49-50 is found in the specification, e.g., page 22, particularly, lines 22-23 of page 22. No new matter has introduced.

Claims 18 and 19 are rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. The Examiner suggests that the claims should be amended to recite that the antibody is isolated and purified to overcome this rejection.

Applicants respectfully submit that the rejection of claims 18 and 19 is rendered moot in view of cancellation of these claims. Applicants further respectfully submit that new claims 36-50 are written to recite an "isolated" antibody. Therefore, withdrawal of the rejection under 35 U.S.C. §101 is respectfully requested.

Claims 18 and 19 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

Applicants respectfully submit that the rejection is moot in view of cancellation of claims 18 and 19. Applicants further submit that new claims 36-50 are not indefinite. Withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is therefore respectfully requested.

Claims 18 and 19 are rejected under 35 U.S.C. §112, first paragraph. The Examiner contends that the specification, while enabling for an antibody which specifically binds the polypeptide consisting of SEQ ID NO: 4 or the polypeptide encoded by the polynucleotide of SEQ ID NO: 3, does not reasonably provide enablement for the scope of the antibodies as claimed.

Applicants respectfully submit that this enablement rejection of claims 18-19 is rendered moot in view of cancellation of these claims. Applicants further submit that new claims 36-50 are fully enabled by the specification. Therefore, withdrawal of the rejection of claims 18-19 under 35 U.S.C. §112, first paragraph (enablement) is respectfully requested.

Claim 18 and 19 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

D

to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

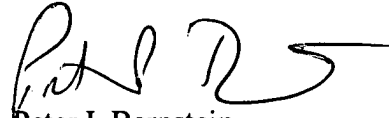
The Examiner observes that the claims are drawn to an antibody which binds a polypeptide having at least two or three of the characteristics disclosed in claims 16 and 17. The Examiner acknowledges that the specification discloses the polypeptide sequence of SEQ ID NO: 4. However, the Examiner contends that the instant disclosure of one polypeptide does not adequately describe the scope of the claimed genus of antibodies, which bind a substantial variety of subgenera including full-length, truncated, fusion polypeptides and variants thereof. The Examiner states that a description of a genus antibodies may be achieved by means of a recitation of a representative number of polypeptides they bind, defined by an amino acid sequence, and a recitation of structural and functional features common to members of the genus.

Applicants respectfully submit that this written description rejection of claims 18 and 19 is moot in view of cancellation of these claims. Applicants further submit that new claims 36-50 fully comply with the written description requirement under 35 U.S.C. §112, first paragraph. Specifically, the antibodies as presently claimed are generated using an IL-13 receptor α -chain polypeptide comprising all or part of SEQ ID NO: 4, which antibody binds to an IL-13 receptor α -chain (claim 36); or binds to an IL-13 receptor α -chain consisting of the sequence of SEQ ID NO: 4 (Claims 37 and 49-50). Therefore, the presently claimed antibodies are adequately described by at least a functional feature (i.e., their binding characteristics). Thus, withdrawal of the written description rejection is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the instant amendment. The attached page is captioned "**Version with Markings to Show Changes Made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Peter I. Bernstein

Registration No. 43,497

Scully, Scott, Murphy & Presser
400 Garden City Plaza
Garden City, New York 11530
Telephone: 516-742-4343

PIB/XZ:ab

Encs.:

- Version with markings to show changes made;
- Substitute computer-readable and paper copy of the Sequence Listing;
- Statement under 37 CFR §1.821(f).

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please replace the paragraph beginning at Page 31, line 10 with the following rewritten paragraph:

[BRIEF DESCRIPTION OF THE FIGURES] **BRIEF DESCRIPTION OF THE DRAWINGS**

[Figure 1 is a representation of] **Figures 1A-1F show** the nucleotide ([[]SEQ ID NO:1[]]) and predicted amino ([[]SEQ ID NO:2[]]) sequence of murine NR4. The untranslated region is shown in lower case and the translated region in upper case. The conventional one-letter code for amino acids is employed, potential asparagine linked glycosylation sites are underlined and the conserved cysteine residues and WSXWS (**SEQ ID NO: 9**) motif of haemopoietin receptor family members are shown in bold. The predicted signal sequence is underlined in bold while the transmembrane domain is underlined with dashes. The sequence shown is a composite derived from the analysis of 8 cDNA clones derived from 3 libraries. The 5'-end of the sequence (nucleotides -60 to 351) is derived from a single cDNA clone but is also present in genomic DNA clones that have been isolated. Boxed region – typical haemopoietin receptor domain, amino acids 118-340.

Please replace the paragraph beginning at Page 31, line 27 with the following rewritten paragraph:

[Figure 3 is a graphical representation depicted] **Figures 3A-3B depict** saturation isotherms of ^{125}I -IL-13 and ^{125}I -IL-4 binding; saturation isotherms depicted as Scatchard plots of

IL-4(°) and IL-13(•) binding to [(A)] COS cells expressing the IL-13R α (NR4) (Figure 3A), [(B)] CTLL cells (Figure 3B) and [(C)] CTLL cells expressing the IL-13R α (NR4) (Figure 3C). Data have been normalized to 1×10^4 COS cells and 1×10^6 CTLL cells and binding was carried out on ice for 2 to 4 hours.

Please replace the paragraph beginning at Page 32, Line 3 with the following rewritten paragraph:

[Figure 4 is a graphical representation showing] Figures 4A-4D show specificity of IL-4 and IL-13 binding; the ability of IL-4(°) and IL-13(•) to compete for ^{125}I -IL-13 binding to [(A)] COS cells expressing the IL-13R α (NR4) (Figure 4A) and [(C)] CTLL cells expressing the IL-13R α (NR4) (Figure 4C) or to compete for ^{125}I -IL-4 binding to [(B)] CTLL cells (Figure 4) and [(D)] CTLL cells expressing the IL-13R α (NR4) (Figure 4). Binding was carried out at 4°C for 2 to 4 hours and the data expressed as a percentage of the specific binding observed in the absence of a competitor (Δ).

Please replace the paragraph beginning at Page 32, line 10 with the following rewritten paragraph:

[Figure 5 is a graphical representation showing] Figures 5A-5B show factor dependent proliferation of cells expressing NR4. Two hundred [(A)] CTLL cells (Figure 5) or [(B)] CTLL cells (Figure 5) expressing the IL-13R α (NR4) were incubated in the absence of cytokine or with various concentrations of IL-2 (\square), IL-4(°) or IL-13 (•). After 48 hours viable cells were counted and data were expressed as a percentage of the number of viable cells observed with a maximal concentration of IL-2.

Please replace the paragraph beginning at Page 32, line 3 with the following rewritten paragraph:

[Figure 7 is a representation of] Figures 7A-7J show the nucleotide and corresponding amino acid sequence of murine SEQ ID NOS: 1 and 2, respectively) and human (SEQ ID NOS: 3 and 4, respectively) NR4 (IL-13R α) genes. The nucleotide and predicted amino acid sequence of human (H) and murine (M) IL-13R α (NR4) were aligned by eye, with gaps (-) inserted to optimize the alignment. The numbering is for the murine clone, nucleotides that form part of the coding region are shown in upper case, whilst those of the untranslated regions are shown in lower case. Amino acids identical between the predicted murine and human proteins are indicated by (*). DNA encoding the murine signal sequence is underlined, with A26 or T27 being the predicted first amino acid of the mature protein.

Please amend the paragraph beginning at page 33, line 12, as follows:

Figure 10 is a representation of the N-terminal amino acid sequence of murine NR4 (SEQ ID NOS: 10 and 11).

Please amend the paragraph beginning at page 37, line 3, as follows:

A library was constructed λ ZAP II using ApoI digested genomic DNA from embryonal stem cells and screened with a pool of 32 P-labelled oligonucleotides encoding the amino acid sequence Trp-Ser-Asp-Trp-Ser (SEQ ID NO: 12) found in many members of the haemopoietin receptor family. One hybridising bacteriophage clone was found to contain a sequence that appeared to encode part of a novel member of the haemopoietin receptor family. This receptor was given the operational name NR4. The sequence of the genomic clone was used to isolate cDNAs encoding NR4 from WEHI-3B cell, peritoneal macrophage, bone marrow, skin and kidney libraries. A composite of the nucleotide sequence ([SEQ ID NO: 1]) and predicted

amino acid sequence ([SEQ ID NO: 2]) of these cDNAs is shown in Figure 1. The NR4 cDNA is predicted to encode for a protein of 424 amino acid residues, containing a putative signal sequence and transmembrane domain. The extracellular region of the protein contained an immunoglobulin-like domain (amino acids 27-117), in addition to a typical haemopoietin receptor domain (amino acids 118-340) which includes four conserved cysteine residues and the characteristic Trp-Ser-Asp-Trp-Ser motif (Figure; in bold as WSXWS). The cytoplasmic tail of the new receptor was 60 amino acids in length.

IN THE CLAIMS:

Please cancel claims 16-19 without prejudice.

Please add the following claims:

36. An isolated antibody generated using an IL-13 receptor α -chain polypeptide comprising all or part of SEQ ID NO: 4, which antibody binds to an IL-13 receptor α -chain.

37. An isolated antibody which binds specifically to an IL-13 receptor α -chain consisting of the sequence of SEQ ID NO: 4.

38. The isolated antibody according to claim 36 or 37, wherein said antibody inhibits the interaction between IL-13 and an IL-13 receptor α -chain.

39. The isolated antibody according to claim 36 or 37, wherein said antibody inhibits the interaction between IL-13 and an IL-13 receptor α -chain consisting of the sequence of SEQ ID NO: 4.

40. The isolated antibody according to claim 36 or 37, wherein said antibody inhibits the interaction between an IL-13 receptor α -chain and an IL-4 receptor α -chain.

41. The isolated antibody according to claim 36 or 37, wherein said antibody is a polyclonal antibody.

42. The isolated antibody according to claim 36 or 37, wherein said antibody is a monoclonal antibody.

43. A pharmaceutical composition comprising the antibody according to claim 36 or 37, and at least one of a pharmaceutically acceptable carrier or a diluent.

44. A pharmaceutical composition comprising the antibody according to claim 38 and at least one of a pharmaceutically acceptable carrier or a diluent.

45. A pharmaceutical composition comprising the antibody according to claim 39 and at least one of a pharmaceutically acceptable carrier or a diluent.

46. A pharmaceutical composition comprising the antibody according to claim 40 and at least one of a pharmaceutically acceptable carrier or a diluent.

47. A pharmaceutical composition comprising the antibody according to claim 41 and at least one of a pharmaceutically acceptable carrier or a diluent.

48. A pharmaceutical composition comprising the antibody according to claim 42 and at least one of a pharmaceutically acceptable carrier or a diluent.

49. An isolated antibody against an IL-13 receptor α -chain or an antigen-binding fragment thereof, wherein said antibody or said antigen-binding fragment binds SEQ ID NO: 4.

50. The isolated antibody or antigen-binding fragment of claim 49, wherein said IL-13 receptor α -chain consists of SEQ ID NO: 4.

D